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June 06, 2003

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APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A
FILING DATE.

APPLICATION NUMBER: 60/376,498

FILING DATE: April 30, 2002

RELATED PCT APPLICATION NUMBER: PCT/US03/13560

By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS



T. Wallace
T. WALLACE
Certifying Officer

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DOCUMENT**

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COMPLIANCE WITH RULE 17.1(a) OR (b)

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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 C.F.R. 1.53(b)(2).

Docket Number

AVIOR-07217

Type a plus sign (+)
inside this box →

INVENTOR(s) / APPLICANT(s)

Last Name	First Name	Middle Initial	Residence (City and Either State or Foreign Country)
Lieber	Andre		Seattle, WA

TITLE OF THE INVENTION (280 Characters Max.)

Kits, Systems, Compositions, and Methods for Dendritic Cell Transduction, Maturation, and Stimulation of Antigen Specific Immune Responses.

CORRESPONDENCE ADDRESS

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
United States of America

ENCLOSED APPLICATION PARTS (Check All That Apply)

<input checked="" type="checkbox"/> Specification	Number of Pages	1	<input type="checkbox"/> Small Entity Statement
<input checked="" type="checkbox"/> Drawing(s)	Number of Sheets	0	<input type="checkbox"/> Other (Specify): Power of Attorney
			<input type="checkbox"/> Other (Specify): Assignment

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

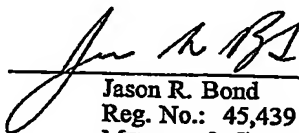
<input type="checkbox"/> Charge Account No. 08-1290 in the amount of \$80.00. An originally executed duplicate of this transmittal is enclosed for this purpose.	FILING FEE AMOUNT (\$)	\$80.00
<input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any deficiency in the payment of the required fee(s) and/or credit any overpayment to Deposit Account No.: 08-1290. An originally executed duplicate of this transmittal is enclosed for this purpose.		

This invention was made by an agency of the United States Government under a contract with an agency of the United States Government.

☒ No.
☐ Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

Date: April 30, 2002


Jason R. Bond
Reg. No.: 45,439
MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
(608) 218-6900

Additional inventors are being named on separately numbered sheets attached hereto.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Andre Lieber

For: Kits, Systems, Compositions, and Methods for Dendritic Cell Transduction, Maturation, and Stimulation of Antigen Specific Immune Responses.

Box Provisional Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

CERTIFICATION UNDER 37 C.F.R. § 1.10

I hereby certify that this correspondence and the documents referred to as attached therein are being deposited with the United States Postal Service on April 30, 2002, in an envelope as "EXPRESS MAIL POST OFFICE TO ADDRESSEE" service under 37 C.F.R. § 1.10, Mailing Label Number EV 092 300 030 US addressed to: Box Provisional Patent Application, Assistant Commissioner for Patents, Washington, D.C. 20231.


Susan M. McClintock

TRANSMITTAL COVER SHEET FOR FILING PROVISIONAL APPLICATION
(37 C.F.R. § 1.51(2)(i))

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 C.F.R. 1.53(b)(2).

1. The following comprises the information required by 37 C.F.R. § 1.51(a)(2)(i)(A):
2. The name(s) of the inventor(s) is/are (37 C.F.R. § 1.51(a)(2)(i)(B)):

Andre Lieber
3. Address(es) of the inventor(s), as numbered above (37 C.F.R. § 1.51(a)(2)(i)(C)):

Seattle, WA
4. The title of the invention is (37 C.F.R. § 1.51(a)(2)(i)(D)):

Kits, Systems, Compositions, and Methods for Dendritic Cell Transduction, Maturation, and Stimulation of Antigen Specific Immune Responses.
5. The name, registration, and telephone number of the attorney (if applicable) is (37 C.F.R. § 1.51(a)(2)(i)(E)):

Jason R. Bond
Reg. No.: 45,439
Tel.: (608) 218-6900

(complete the following, if applicable)

— A Power of Attorney accompanies this cover sheet.

6. The docket number used to identify this application is (37 C.F.R. § 1.51(a)(2)(i)(F)):

Docket No.: AVIOR-07217

7. The correspondence address for this application is (37 C.F.R. § 1.51(a)(2)(i)(G)):

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105

8. Statement as to whether invention was made by an agency of the U.S. Government or under contract with an agency of the U.S. Government. (37 C.F.R. § 1.51(a)(2)(i)(H)):

This invention was made by an agency of the United States Government, or under contract with an agency of the United States Government.

X No.

— Yes.

The name of the U.S. Government agency and the Government contract number are:

9. Identification of documents accompanying this cover sheet:

- A. Documents required by 37 C.F.R. § 1.51(a)(2)(ii)-(iii):

Specification: No. of pages 1

Drawings: No. of sheets 0

- B. Additional documents:

— Claims: No. of claims

— Power of Attorney

— Small Entity Statement

— Assignment

— Other

10. Fee

The filing fee for this provisional application, as set in 37 C.F.R. § 1.16(k), is \$160.00, for other than a small entity, and \$80.00, for a small entity.

X Applicant is a small entity.

11. Small Entity Statement

— The verified statement(s) that this is a filing by a small entity under 37 C.F.R. §§ 1.9 and 1.27 is(are) attached.

12. Fee payment being made at this time

— Charge Account No. 08-1290 in the amount of \$80.00. An originally executed duplicate of this transmittal is enclosed for this purpose.

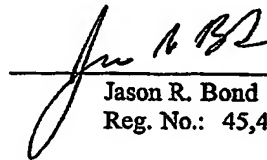
13. Method of Fee Payment:

X Check in the amount of \$80.00

— Charge Account No. 08-1290, in the amount of \$80.00. A duplicate of this Cover Sheet is attached.

X Please charge Account No. 08-1290 for any fee deficiency. A duplicate of this Cover Sheet is attached.

Date: April 30, 2002



Jason R. Bond
Reg. No.: 45,439

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60376498-043002

Kits, Systems, Compositions, and Methods for Dendritic Cell Transduction, Maturation, and Stimulation of Antigen Specific Immune Responses.

Transduction of Human CD34+ Peripheral Blood Derived Dendritic Cells with a Model Tumour Antigen is More Efficient with Chimeric Ad5/11 and Ad5/35 Adenoviruses than Ad5

In order to use dendritic cells as immunotherapy vectors, an efficient method of antigen delivery is essential. Subgroup C (serotype 5) based adenovirus vectors have successfully been used to transduce human dendritic cells (DC) in culture, however the need for high MOI's and the resulting toxicity has hindered their use. Following our previous observation that Ad 5 based vectors possessing group B fibers (Ad11 and Ad35) give increased transduction over Ad5 vectors in human hematopoietic cells without abhorrent toxicity, we investigated the transduction efficiencies of these vectors in human hematopoietic derived DCs. Infection of immature CD11c positive DCs derived from peripheral CD34+ cells, with Ad5, Ad5/11 and Ad5/35 vectors expressing GFP resulted in <1%, 59% and 37% transduction at an MOI of 5. Maximal transduction efficiency with Ad5/11 and Ad5/35 vectors (85-95%) was achieved at a MOI 100 whilst only 58% transduction was achieved with the highest Ad5 dose tested (MOI 1000). Expression of the DC maturation markers CD86, CD83 and HLA-DR was seen to increase upon Ad5/11 and Ad5/35, but not Ad5 infection, 24 hours after infection. Furthermore introduction of the maturation factor (LPS) to infected DCs resulted in an increased percentage of cells expressing GFP following Ad5/11 and Ad5/35, but not Ad5, infection. Ad5 and Ad5/35 vectors were then generated expressing a model tumour antigen (Hepatitis B nucleocapsid, HBeAg) from a *RETROGEN* cassette that contains an N-terminal leader sequence and a C-terminal human Fc binding domain. Ad5/35 infected CD11c positive DCs showed enhanced expression of HBeAgFc compared to the Ad5 infected cells. Ad5 and Ad5/35 HBeAgFc infected DCs were then incubated with antigen loaded autologous peripheral T cells. Enhanced T cell proliferation and secretion of the Th1 cytokine IFN- γ was seen in T cells incubated with Ad5/35HBeAgFc infected DCs compared to Ad5HBeAgFc infected cells. Taken together these results indicate that group B pseudotyped adenoviruses enable more efficient DC transduction, maturation and stimulation of antigen specific immune responses at lower, not toxic MOIs.